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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,048	09/20/2007	Robert R. Rando	HMV-091.02	9518

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EXAMINER
SZNAIDMAN, MARCOS L

ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/598,048	RANDO, ROBERT R.	
	Examiner	Art Unit	
	MARCOS SZNAIDMAN	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *271-276* is/are pending in the application.

4a) Of the above claim(s) *274 and 275* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *271-273 and 276* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8 pages / 05/24/07, 05/24/07, 12/07/07, 02/01/08 and 10/17/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to applicant's reply filed on July 17, 2009.

Election/Restrictions

Applicant's election of macular degeneration as the species for ophthalmologic disorders in the reply filed on July 17, 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a).

Status of Claims

Cancellation of claims 277-279 is acknowledged

Claims 271-276 are currently pending and are the subject of this office action.

Claims 274-275 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on July 17, 2009.

Claims 271-273 and 276 are presently under examination.

Priority

The present application is a 371 of PCT/US05/004990 filed on 02/17/2005, and claims priority to provisional application No. 60/578,324 filed on 06/09/2004, No. 60/567,604 filed on 05/03/04 and 60/545,456 filed on 02/17/04.

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Applications No. 60/545,456 and 60/567,604, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Application 60/545,456 and 60/567,604 fail to disclose the use of fenretinide. Accordingly, none of the examined claims (271-273 and 276) are entitled to the benefit of the prior applications. The priority date for all the claims is 06/09/2004 corresponding to provisional application No. 60/578,324.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 271-273 and 276 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating macular degeneration (species elected) comprising administering an effective amount of fenretinide, does not reasonably provide enablement for preventing macular degeneration (species elected) comprising administering an effective amount of fenretinide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. This is a scope of enablement rejection.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fd. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996). As pointed out by the court in *In re Angstadt*, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth *In re Wands*, 8 USPQ2d 1400

(CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547 the court recited eight factors:

1- the quantity of experimentation necessary,

2- the amount of direction or guidance provided,

3- the presence or absence of working examples,

4- the nature of the invention,

5- the state of the prior art,

6- the relative skill of those in the art,

7- the predictability of the art, and

8- the breadth of the claims

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the *Wands* factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention

Claims 271-273 and 276 recite a method of treating or preventing macular degeneration (species elected), comprising administering to a subject a pharmaceutically acceptable amount of fenretinide or a pharmaceutically acceptable salt thereof.

2. The relative skill of those in the art

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. The artisan using Applicant's invention would generally be a physician with a M.D. degree and several years of experience.

3. The state and predictability of the art

As illustrative of the state of the art regarding the treatment or prevention of macular degeneration, the Examiner cites: Comer et. al. (Expert Opinion on Emerging Drugs (2005) 10:119-135).

Comer teaches that single effective treatment strategy is still limited by a lack of full understanding of the underlying disease etiology (see page 120 under Medical need). However, the state of the art appears to be silent regarding the prevention of macular degeneration. Prevention is considered a synonymous with the term curing and both circumscribe methods of treatment having absolute success.

4. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides data that proves the fenretinide binds to purified RPE65. However, the specification does not provide any study that the administration of fenretinide or any other close analog could prevent macular degeneration.

5. The quantity of experimentation necessary

Because of the known unpredictability of the art (as discussed in section 3) and in the absence of experimental evidence commensurate in scope with the claims (as discussed in section 4), the skilled artisan would not accept that fenretinide could be predictably be used to prevent macular degeneration.

6. Conclusion

Accordingly, the inventions of claims 271-273 and 276 do not comply with the scope of enablement requirement of 35 U.S.C 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation, with no reasonable expectation of success.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 271-273 and 276 is rejected under 35 U.S.C. 103(a) as being unpatentable over Campochiaro et. al. (US 6,075,032) in view of Fanjul et. al. (The Journal of Biological Chemistry (1996) 271:22441-22446).

Claims 271-273 and 276 recite a method of treating or preventing macular degeneration (species elected) in a subject with macular degeneration (see 112 2nd above), comprising administering to the subject a pharmaceutically acceptable amount of fenretinide or a pharmaceutically acceptable salt thereof.

For claims 271 and 273 Campochiaro teaches the treatment of ocular diseases associated with choroidal neovascularization, such as related macular degeneration

with a therapeutically effective amount of a Retinoic Acid Receptor (RAR) agonist which is also a potent antagonist of AP1-dependent gene expression (see abstract and also claims 1-2, 4 and 5).

Campochiaro does not teach the treatment of macular degeneration with fenretinide. However, Fanjul teaches that fenretinide (4-hydroxyphenyl retinamide or 4HPR) is a selective RAR agonist with anti AP-1 activity (see for example Abstract, also under Results on page22442, also page 22443 under *4HPR Transrepression selectivity is distinct from its transactivation*, and on page 22445 under discussion, second paragraph).

Since Campochiaro et. al. teach a method of treating macular degeneration with a RAR agonist that also antagonizes AP-1, and since Fanjul et. al. teach that fenretinide is a RAR agonist that also antagonizes AP-1, at the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to substitute one functional equivalence (any RAR agonist that also antagonizes AP-1) for another (fenretinide) with an expectation of success, since the prior art establishes that both function in similar manner.

Although the prior art is silent regarding the statement in claims 272: "wherein fenretinide inhibits, antagonizes, or short circuits the visual cycle at a step of the visual cycle that occurs outside a disc of a rod photoreceptor cell" and claim 276: "wherein fenretinide increases the rate at which 11-cis-retinal is isomerized to all-trans-retinal; inhibits, antagonizes, or short circuits the visual cycle in the retinal pigment epithelium; inhibits at least one of lecithin retinol acyl transferase, isomerohydrolase, and 11-cis-

retinol dehydrogenase, or inhibits binding to RPE65", these limitations do not result in a manipulative difference with the prior art and will necessary be present in the method made obvious by Campochiaro and Fanjul (see above), since the same compound: fenretinide is being used to treat the same disease: macular degeneration.

In other words, products of identical or similar composition cannot exert mutually exclusive properties when administered under the same circumstances. MPEP 2112 I states: "The discovery of a previously unappreciated property of a prior art composition or a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer".

All this would result in the practice of claims 271-273 and 276 with a reasonable expectation of success.

Conclusion

No claims are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571-272-0580. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1612
February 25, 2008

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612